

Remarks

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

Initially, applicants would like to note that the present amendment is being submitted in compliance with “Amendments In A Revised Format Now Permitted”, 1267 OG 4 (February 25, 2003). Pursuant to this notice, the requirements of 37 C.F.R. § 1.121 have been waived.

The rejection of claims 1-7 under 35 U.S.C. § 102(b) as being anticipated by Huc et al., “Virtual Combinatorial Libraries: Dynamic Generation of Molecular and Supramolecular Diversity by Self-Assembly,” Proc. Nat’l Acad. Sci. USA 94:2106-2110 (1997) (“Huc”) is respectfully traversed.

Huc teaches the formation of a combinatorial library formed by reacting aldehydes 1, 2, or 3 with amines a, b, c, or d to form imines (see Figure 2 and page 2108, first column). To this combinatorial library, carbonic anhydrase II (“CA”) was added to identify those library members that can bind with affinity to CA (see page 2108, first column). Although Huc indicates that CA itself possesses a Zn(II) ion—it is, after all, a metalloproteinase—the Zn(II) ion is not a component of the combinatorial library. Instead, it is a component of the biological receptor or target. The members of Huc’s combinatorial library are the imines themselves, not coordination complexes that are each “formed of a metal atom or metal ion and at least two non-biopolymer ligands” where “each of the at least two non-biopolymer ligands is reversibly bonded through the at least one functional group thereof to the metal atom or metal ion by a labile coordinate bond and wherein each different complex in said library has different ligands bonded to the metal atom or metal ion.” Even if the Zn(II) ion is considered (albeit inappropriately) as a member of the complex formed between the imine and the CA target, Huc does not teach or suggest that the Zn(II) ion (which is complexed by the CA metalloproteinase) complexes with at least two imines of Huc. Thus, even according to the interpretation proposed by the U.S. Patent and Trademark Office (“PTO”), the only complex formed with the Zn(II) ion contains a single imine and CA itself, which is not a non-biopolymer ligand as presently claimed. Because Huc fails to teach or suggest each and every limitation of the presently claimed invention, Huc cannot anticipate claims 1-7. Therefore, the rejection of claim 1-7 is improper and should be withdrawn.

The rejection of claims 1-7 and 10 under 35 U.S.C. § 103(a) for obviousness over Huc alone or in view of U.S. Patent No. 5,958,702 to Benner et al. ("Benner").

The teachings of Huc and its deficiencies are set forth above.

Benner discloses a combinatorial library which contains two components (Ax and yB), each including a functional group which allows the two components to react directly together when presented with a ligand (see column 5, lines 26-61). In Example 5, however, Benner discloses the introduction of a borate ion into a solution which includes a beta lactamase and 1,2 diols, where the 1,2 diols react with the borate ion to form a combinatorial library of borate esters or orthoborate esters. However, this aspect of Benner does not even involve a metal atom or metal ion and the diols do not form a labile coordinate bond with a metal atom or metal ion.

The PTO cites to Benner merely for the motivation to "scale up" of the library in Huc to create a library of the type disclosed in claim 10 (see office action at pages 5-6). However, the PTO has not demonstrated how Benner overcomes the above-noted deficiencies of Huc and applicants submit that Benner fails to do so. For this reason, the combination of Huc and Benner cannot teach or suggest each and every limitation of the presently claimed invention. Therefore, the rejection of claims 1-7 and 10 is improper and should be withdrawn.

Claims 1-7 and 10 are rejected under 35 U.S.C. § 102(e) as anticipated by, or alternatively under 35 U.S.C. § 103(a) for obviousness over, U.S. Patent No. 5,976,887 to Bruno et al. ("Bruno") in view of page 10 of the specification.

The effective date of Bruno under 35 U.S.C. § 102(e) is June 2, 1997. As evidenced by the accompanying Declaration of Benjamin L. Miller under 37 CFR § 1.131 ("Miller Decl."), the presently claimed invention was reduced to practice in the United States prior to June 2, 1997. For this reason, Bruno is not available as prior art. Therefore, the rejection is improper and should be withdrawn.

Claims 1-7 and 10 are rejected under 35 U.S.C. § 103(a) for obviousness over WO 98/12156 to Jacobsen et al. ("Jacobsen") in view of Huc alone or further in view of Benner.

The cited effective date of Jacobsen under 35 U.S.C. § 102(a) is March 26, 1998. Even if Jacobsen is entitled (as a PCT designating the U.S.) to an effective date under 35 U.S.C. § 102(e), that date would not be any earlier than September 19, 1997. Regardless

of the effective date of Jacobsen, the accompanying Miller Decl. evidences that the presently claimed invention was reduced to practice in the United States prior to June 2, 1997. Therefore, Jacobsen is not available as prior art. Because Jacobsen is not available as prior art and the combination of Huc and Benner is deficient for the reasons noted above, the rejection of claims 1-7 and 10 for obviousness over Jacobsen in view of Huc alone, or further in view of Benner, is improper and should be withdrawn.

The rejection of claims 1-7 and 10 under 35 U.S.C. § 103(a) for obviousness over U.S. Patent No. 5,157,032 to Barton et al. ("Barton") in view of Huc alone, or further in view of Benner, is respectfully traversed.

Barton discloses the preparation of coordination complexes having the formula $M-(R_1)(R_2)(R_3)$, where M is a transition metal (defined at col. 9, line 67 to col. 10, line 2) and each of R_1 , R_2 , and R_3 is a ligand group as defined at col. 10, lines 4-19. R_1 and R_2 are disclosed as being the same or different and, when the same, they are different from R_3 . Barton further discloses that these complexes can be used to label double stranded DNA.

Barton never discloses or suggests the formation of a combinatorial library that exists in aqueous solution (particularly at equilibrium with the metal ions and ligands that form such complexes). Barton merely prepares the coordination complexes individually and under non-aqueous (and often denaturing) conditions (see each separate description for the preparation of complexes under Examples I-III).

Equally as important is the fact that (contrary to the PTO's suggestion at page 11 of the outstanding office action) the complexes formed by Barton are not characterized by the presence of a labile bond between the ligand and the transition metal ion. The resulting coordination complexes are stable di- or tri-cations—they are described as chloride salts in the Examples—and therefore would not be expected to exist at equilibrium with the component transition metal ions and ligands when introduced into an aqueous environment.

The teachings of Huc and Benner are set forth above.

The PTO has merely asserted at pages 11-12 of the outstanding office action that it would have been obvious to one of ordinary skill in the art to prepare the combinatorial library of Barton using receptor assisted combinatorial chemistry of Huc or Benner. Applicants respectfully disagree.

First of all, because the reaction conditions for formation of the individual complexes prepared separately by Barton (and not as a combinatorial library) all involve one or more steps that require non-aqueous and/or denaturing conditions, one of ordinary skill in

the art would not have even been motivated to attempt to prepare any one complex, let alone a whole library thereof, using receptor assisted combinatorial chemistry. The receptor for the complexes of Barton is double stranded DNA, which would not survive the reaction protocols described by Barton. Thus, not only does Barton teach away from combinatorial chemistry in general (most examples required different conditions), but Barton certainly teaches away from receptor assisted combinatorial chemistry given that the dsDNA could not tolerate the non-aqueous and/or denaturing conditions used during synthesis.

Secondly, even if one of ordinary skill in the art were to have conducted receptor assisted combinatorial chemistry to prepare Barton's complexes (i.e., using some unknown aqueous conditions that Barton fails to identify), Barton does not provide any evidence that labile bond formation between the transition metal ions and ligands would occur. Because none of the references describe the reaction conditions that would even allow a combinatorial library of the various Barton coordination complexes to form, one of ordinary skill in the art would have no expectation that such complexes, even if they were to form, would contain a labile bond. Therefore, the combination of Barton in view of Huc and Benner fails to provide any expectation of success.


Finally, given the fact that none of the references teach the preparation of a combinatorial library whose members possess a labile bond formed between a metal atom or ion and "each of the at least two non-biopolymer ligands", let alone that such complexes in the library exist under aqueous conditions and at equilibrium with the metal atoms or metal ions and the non-biopolymer ligands, the combination of Barton, Huc, and Benner fails to teach or suggest each and every limitation of the presently claimed invention.

For all of these reasons, the rejection of claims 1-7 and 10 for obviousness over Barton in view of Huc alone, or further in view of Benner, is improper and should be withdrawn.

In view of all the foregoing, it is submitted that this case is in condition for allowance and such allowance is earnestly solicited.

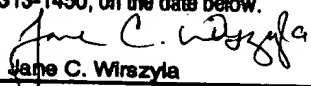
Respectfully submitted,

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